PSJ2 Exh 17

ADDENDUM

1. In the first paragraph of the letter, it is stated that "Addiction is a real, present and growing danger." While OxyContin has an abuse potential similar to morphine, as you correctly state, that does not equate to a high rate of addiction – when the medication is taken as directed. As Dr. Alan Leshner, Executive Director of the National Institute of Drug Abuse (NIDA), stated on April 10, 2001, "Many studies have shown...that properly managed medical use of opioid analgesic drugs is safe and rarely causes clinical addiction."

2. The letter notes that non-cancer patients are the "main recipients of such opioid painkillers." This is indeed a fact. The reason for this is that moderate-to-severe chronic non-malignant pain is a very serious problem in the United States affecting far more people than is the pain associated with malignant disease. The American Pain Foundation estimates that over 50,000,000 people in the U.S. suffer from pain. Moreover, under treated pain has been recognized by the medical community and government, at both State and Federal levels, as a major health crisis. Responsible medical authorities and government bodies are advocating aggressive efforts to reach out to those who are suffering with debilitating pain and treat them. Such treatment, in appropriate cases, includes treatment with opioid analgesics such as OxyContin tablets. As stated by the American Academy of Pain Medicine in its press release of February 16, 2001, "The public health problem represented by misuse of prescription opioids is miniscule in comparison with that of untreated and unrelenting pain."

3. The letter quotes the *Sunday New York Times Magazine* as reporting that family physicians account for 21 percent of the physicians who prescribe OxyContin Tablets. There are only four to five thousand pain specialists in the United States, according to the American Academy of Pain Medicine. The vast majority of pain treated in this country – particularly cancer pain – is under the direction of primary care physicians. Most often when cancer is diagnosed, even at a major urban cancer center, pain control for the patient falls to the hands of the patient's family physician.

4. The letter notes that Connecticut's Chief Medical Examiner has reported 16 deaths related to oxycodone in 1999 and 26 in 2000. Purdue has a legal obligation to investigate and report deaths attributed to our product to the FDA. In over 90% of the cases we have examined, deaths among abusers are caused by multiple drug toxicity, usually including alcohol. We would appreciate your assistance in requesting the Connecticut Medical

Examiner to share that data with us so that we may conduct an independent investigation and make our report to the FDA.

5. Regarding the "growing addiction to OxyContin, whether acquired illegally or prescribed", the fact is that there are simply no data to support a conclusion that the rate of addiction among patients is "growing." This is so, notwithstanding the efforts of the press and plaintiffs' attorneys in litigation against the Company to produce individuals who claim to have become addicted to OxyContin. As for addiction among those who have illicitly obtained the drug, clearly there are no data at all. Most law enforcement officers and substance abuse professionals with whom we have spoken advised us that the vast majority of those who are currently addicted to OxyContin have previously abused or have been addicted to other legal and illegal drugs.

6. Reference is made to "the astonishing growth in state funding for OxyContin prescriptions...." We believe that it is an error to assume that the increase in the use of the drug is a consequence of illegal abuse and diversion. There are many reasons for this growth. We believe that growth represents legitimate and appropriate treatment of patients in pain. Our data show that the rate of increase in the use of our drug among individuals receiving various forms of public assistance does not exceed the rate of increase among the general population. It is well known that there are many factors that have led to the dramatic increase in utilization of all opioid analgesics in the last decade. These include the following:

- New national standards for pain management issued by the Joint Commission on Accreditation of Healthcare Organizations took effect on January 1, 2001. These evidence-based pain management standards require nearly 18,000 accredited hospitals and other health care facilities to make pain management an integral part of all treatment plans.
- Newly created laws, such as various intractable pain acts, have been adopted in many states, which provide physicians with support for the use of opioids in the management of pain.
- The American Bar Association issued a progressive policy on the use of opioids. The ABA resolution provided that "federal, state, and territorial governments should construe, apply, and if necessary, amend laws regulating the health professions, controlled substances, insurance, in both public and private health benefit programs, so that these laws do not impose barriers to quality pain and symptom management." The ABA further resolved that "federal, state, and territory governments should support the rights of individuals suffering from pain to be informed of, choose, and receive effective pain and symptom evaluation management and ongoing monitoring as part of basic medical care."

- Congress passed a resolution declaring this the Decade of Pain Control and Research.

We believe that it would be wrong, discriminatory and bad public policy to deprive appropriate patients receiving public assistance of the proper medicines that are available to those who can pay for them.

7. We note that the letter advocates legislation to establish a state electronic prescription monitoring program (PMP). As you know from our discussion of this subject, we totally support that effort and have been advocating that other states to adopt such programs. We recently met with Attorney General Mike Moore of Mississippi who is one of the most knowledgeable public officials regarding PMPs. We hope to draw on his expertise as we work to develop a model PMP. Similarly, Congressman Jim Greenwood, chair of the House Energy and Commerce Committee's Subcommittee on Investigation, also expressed an interest in considering a role for the Federal government in such programs. We would be eager to discuss with you the insight we have on this subject.

8. The letter states that "while Purdue Pharma seems sincere in seeking to address the problems, no comprehensive effective solutions have yet been offered." We believe the opposite is true: no pharmaceutical company has ever offered more by way of specific, focused and effective programs to deal with the public health problem of prescription drug abuse. Those in law enforcement who have been most deeply affected by the problem and have worked with us, have repeatedly praised us on the effectiveness and seriousness of our programs. In this regard, I would urge you to speak with former Maine U.S. Attorney Jay McCloskey. Mr. McCloskey worked as a federal prosecutor fighting drug diversion and abuse for over 20 years. While U.S. Attorney, he worked with Purdue in Maine (the first state where the problem was reported) and in his view, the programs we instituted together in that State appear to be reversing the problem. After he resigned from office, he offered to continue to work with Purdue on efforts to combat abuse and diversion of our drug in Maine and elsewhere. Let him give you his views on how sincere and effective the programs we have developed are. His office number is 207-947-0178.

Similarly, in Kentucky, one of the hardest hit parts of the nation, we have worked with former U.S. Attorney Joseph Famularo. Mr. Famularo achieved national attention in February when he led a sweep resulting in the arrests of over 200 drug traffickers. Please speak with Mr. Famularo and get his view of the efforts we have made together with him in the State of Kentucky to deal with the problem of abuse of our drug and other prescription drugs. Mr. Famularo is still involved in law enforcement and is also a consultant to Purdue on drug diversion issues. He can be reached at 859-873-4797.

Press reports have characterized Lee County, Virginia as "ground zero" for OxyContin abuse in the United States. For many months we have been working with Lee County Sheriff Gary Parsons to develop programs that are of specific application to Lee County. He advised me that the problem of OxyContin abuse in Lee County is declining. I urge you to speak with Sheriff Parsons and ask him about our sincerity and the effectiveness of our programs. The Sheriff can be reached at 540-346-7753.

9. The letter references programs such as tamper proof pads, and drug abuse prevention programs for teens and suggest that these programs fail to address the fundamental serious risk inherent in the drug. You state that "each addresses only a small source of the abuse problem." This is incorrect. I urge you to speak with law enforcement officers in each state where there is a significant problem of the abuse of our drug. Each will tell you (as they have told us) that the major sources of the problem are:

   (a) Doctor shopping and inappropriate prescriptions written by physicians;

   (b) Forged or altered prescriptions; and

   (c) The need to educate young people as to the dangers of prescription drug abuse.

   With the guidance of people who we believe are most knowledgeable, we have concentrated our efforts in the 3 areas where they feel there is the most need. It is again distressing when media such as *The New York Times Sunday Magazine* trivialize these programs which are regarded by true experts as of extreme importance and value not merely "cosmetic and symbolic steps" as you characterize them.

10. The letter makes reference to the changes in the warnings appearing in the OxyContin Tablet package insert and to the "Dear Health Care Professional" letter we mailed to 800,000 doctors last month. It should be noted that it was Purdue who reached out first to FDA to suggest changes in the labeling. The changes are intended to help solve this problem. The warning language referred to in the letter was proposed and substantially written by Purdue.

11. The letter requests that Purdue "overhaul and reform its marketing practices, eliminating the videos and other promotional materials aimed at persuading patients to pressure doctors into prescribing the prescription drug." We are at a loss to understand this reference. We are proud of the efforts we have made to bring to the attention of physicians and patients of the epidemic of untreated pain in the United States today. While Purdue has engaged in a number of un-branded efforts to alert patients to the availability of medications to treat pain, we are aware of nothing that we

have ever produced which encourages patients to "pressure" or even suggest to physicians that OxyContin is more appropriate than another drug for the particular patient. We have never promoted OxyContin to patients. In our efforts to improve pain treatment in the U.S. and elsewhere, we are joined by the weight of medical opinion, and by Federal and State governments. It has been our view that non-promotional and non-product specific activities in this regard are clearly in the public health interest. We would hope that at our meeting you would want to discuss with us efforts you can make to join in this important effort.

12. The letter states that OxyContin "is more powerful, more addictive, more widely sold, more illicitly available, and more publicized than almost any other painkiller." We know of no evidence to even suggest that OxyContin is "more addictive", or "more illicitly available" than other opioid analgesics. On the contrary, available evidence establishes that illicit use of other opioid analgesics such as hydrocodone is far greater than that of OxyContin and, as the FDA and other authorities recognize, oxycodone has no greater potential to addict than does morphine, fentanyl and other opioid analgesics.

13. We are pleased that you recognize the value of the modified new warnings that we have voluntarily put on our package insert. We, too, are pleased with this change. As you may be aware, in its "Talk Paper" posted on the FDA website, the FDA encouraged all manufacturers of opioid analgesics to follow our lead and to review voluntarily and revise as necessary the labeling to similarly emphasize the warnings and precautions and to promote responsible prescribing practices. We are proud to have led the way and agree with you that the industry should follow. We have been told by a number of government officers that the programs we have adopted to combat the abuse and diversion of OxyContin tablets could form a model for the industry to follow.

14. The suggestion of "limited distribution [of OxyContin] through a central pharmacy" would do little if anything to help prevent diversion. On the contrary, it would create additional opportunities for diversion and most importantly, place additional burdens on the truely innocent victims of diversion, the millions of patients in pain. Early on in our meetings with the DEA, that Agency suggested that we study and consider this as a method of reducing abuse and diversion of the product. We carefully studied that proposal and have concluded that central pharmacies are unlikely to have a material effect on the primary sources of OxyContin diversion, and are likely to create additional problems for the following reasons:

    - Central pharmacies would not prevent corrupt or poorly trained doctors from writing inappropriate prescriptions.

- They would do little to prevent prescription forgery and alteration.
- They would have little effect on "doctor shopping."
- They would not help to curb illegal import of OxyContin from Mexico or Canada.
- They would have no impact on OxyContin shipped by unscrupulous off shore Internet pharmacies.
- They would not prevent patients from selling a portion of their medication.
- They would not prevent family members from stealing and re-selling a patient's medication.

While central pharmacies might indeed reduce the number of pharmacy robberies, that benefit is counter-balanced by exposing to risk of robbery the central pharmacies which would be known to hold large inventories of OxyContin. In addition, delivery to patients by central pharmacies would be by mail or common carrier. This would increase the risk of mailbox theft and other forms of in-transit theft. Eliminating the availability of OxyContin at local pharmacies would also eliminate pharmacists dealing with customers they know (a deterrent to fraud) and substitute a system where all the patients are strangers to the dispensing pharmacist.

Beyond all this, and perhaps most important, distribution through central pharmacies would significantly increase the burden on patients who have a legitimate need for these medications.

- Patients in pain would have to suffer – sometimes for days – while waiting mail or common carrier delivery of their medication.
- Patients would be unable to quickly renew their prescriptions if they run out of medication.
- Physicians would have difficulty altering dosing regimens because of the lag time between prescribing and receipt of medication by the patient.

It is for these reasons that those in law enforcement who have had the most direct experience fighting the diversion of OxyContin tablets do not favor central pharmacies. As Purdue considered this suggestion, we sought the opinions of two law enforcement officials who are among the most experienced and knowledgeable about the problem, Joseph Famularo, then United States Attorney for the Eastern District of Kentucky, and Gary Parsons, Sheriff of Lee County, Virginia.

In a letter to Purdue dated May 10, 2001, then U.S. Attorney Mr. Famularo said:

"I am of the opinion that it [restricting the distribution of OxyContin through central pharmacies] would not have a material effect on

OxyContin [ab]use. That opinion is based on my own extensive experience with OxyContin abuse and I have also consulted my two Assistant U.S. Attorneys who worked the OxyContin cases, and continue to actively prosecute drug cases in our London, Kentucky office. I also spoke with the Kentucky State Police Captain at Hazard, Kentucky, who concurred with my opinion. My Health Care Fraud Investigator has contacted the Western District of Virginia Health Care Fraud Investigator and they are of the same opinion."

A copy of Mr. Famularo's letter is attached for your convenience.

Sheriff Parsons, a member of the Virginia Task Force on Prescription Drug Abuse, has had as much experience in this area as any law enforcement officer in the country. In a telephone conversation with him on May 11, 2001 Sheriff Parsons told me that a central pharmacy was a "bad idea" which would "do nothing to help solve the problem" and would only make it harder for legitimate patients to obtain their medications.

15. The letter recommends our restricting sales to physicians "with a specialized need and experience to prescribe the drug". It has been widely reported in the press that DEA supports the restriction of the right to prescribe OxyContin to "pain specialists." From our numerous conversations with the DEA, however, it is clear that these press reports are erroneous and that both the DEA and Purdue have the identical view on this subject: OxyContin tablets (as well as other strong opioids) should only be prescribed by physicians who have experience in their use and who know who to use them. The DEA does not propose that the right to prescribe opioids be limited to "pain specialists." The reality in the United States is that there are very few pain specialists available to treat the vast majority of the patients who need pain treatment. Purdue's sales professionals call only on physicians who have in the past written prescriptions for opioid analgesics. In other words, the doctors we see are already writing prescriptions for drugs of this type. The efforts of our sales force include providing important educational information to assist these doctors in appropriately using drugs like OxyContin. An example of this is our Opioid Assessment and Document Kit which we have distributed to physicians. The purpose of this material is to aid in proper patient selection and to facilitate compliance with prevailing licensing board medical documentation requirements.

16. The discussion of a physician certification program is interesting, but may be beyond the authority or ability of any pharmaceutical company. As you know, we provide many programs which teach the proper use of opioids, including their dangers and benefits. Most of these programs are held locally in hospitals and clinics.

The reference to "seminars in Florida or Arizona to encourage more OxyContin prescriptions" is unclear. As we told you during one of our meetings, in the past we have held meetings in which we trained physicians to be speakers on the subject of proper treatment of pain and proper use of all opioids. Some of these meetings did take place in resort areas. These meetings were intensive, business-oriented meetings conducted in a highly professional manner. We reject the charges that have appeared in some newspapers that our programs were similar to those of other pharmaceutical companies which have been the subject of criticism. In any event, we have not conducted even these professional meetings since the fall of 2000 since we did not want even the perception of improper marketing practices.

The idea of certifying or accrediting physicians who have attended these programs is of interest to us. I would think, however, that the concept of a pharmaceutical company certification might be a problem for some health care professionals. The letter states: "Purdue could require such certifications prior to selling the pharmaceutical to any physician." This would create a number of problems in areas where there is a need to inform and assist physicians who do not have access to such programs, or do not have the time or inclination to participate in them. This is a complex but interesting subject which we would like to explore further with you. In any event, our sales efforts have focused on physicians who were significant prescribers of other opioid analgesics.

17. The letter suggests that Purdue "should adopt a plan that incorporates this approach (the use of Physician Risk Management Plans) for pain management and require a physician's acceptance to such a 'contract'". As you know, we have been working with the FDA for many months on developing a risk management plan for OxyContin, as well as other drugs currently under review by FDA. The new package insert was developed collaboratively by Purdue and the FDA. The role of OxyContin in pain treatment is discussed under the INDICATIONS AND USAGE section, which reads as follows:

"OxyContin Tablets are a controlled-release oral formulation of oxycodone hydrochloride indicated for the management of moderate to severe pain when a continuous, around-the-clock analgesic is needed for an extended period of time.

OxyContin is **NOT** intended for use as a prn analgesic.

Physicians should individualize treatment in every case, initiating therapy at the appropriate point along a progression from non-opioid analgesics, such as non-steroidal anti-inflammatory drugs and acetaminophen to opioids in a plan of pain management such as outlined by the World Health Organization, the Agency for Healthcare Research and Quality

(formerly known as the Agency for Health Care Policy and Research), the Federation of State Medical Boards Model Guidelines, or the American Pain Society.

OxyContin is not indicated for pain in the immediate postoperative period (the first 12-24 hours following surgery), or if the pain is mild, or not expected to persist for an extended period of time. OxyContin is only indicated for postoperative use if the patient is already receiving the drug prior to surgery or if the postoperative pain is expected to be moderate to severe and persist for an extended period of time. Physicians should individualize treatment, moving from parenteral to oral analgesics as appropriate."

We believe that this represents FDA's best thinking as to the role of OxyContin in the treatment of moderate to severe pain.

18. The letter suggests that we consider devoting resources to treatment and rehabilitation programs. However, based upon our interviews with people who are most knowledgeable and most involved in the problem of prescription drug abuse, we are convinced that our funds should be focused in other areas more likely to provide long-term solutions to the problems of drug abuse. It is our preference to apply those funds to educational programs helping physicians and medical students to avoid being part of the problem, and to educate young people as to the dangers of drug abuse. Our success in these areas should eventually reduce the demand for drug treatment and rehabilitation centers.

19. The letter does not appear to regard the tamper resistant prescription pads, which we are now distributing in 16 states, as a significant contribution to solving the problem of diversion. Perhaps this is not an issue in Connecticut, but please be assured that law enforcement officers in many other jurisdictions have told us that this is making an enormous contribution to solving the problem of diversion of our product and other controlled substances. They do not regard this as a "very small part of the overall problem" as you state. They believe that these are a major tool to combat prescription tampering, fraud and counterfeiting.

20. The letter comments on a statement in Purdue's "Partners Against Pain" Internet site and says the following:

"I am disturbed by the site's statement that addiction from prescribed opioids is 'rare in patients without a history of drug/alcohol abuse' if prescribed under a physician's care. This statement is simply not true."

With respect to the frequency of addiction you should be aware that just

last month, in its review of this issue, FDA approved the following language in the OxyContin package insert:

"Concerns about abuse, addiction and diversion should not prevent the proper management of pain. The development of addiction to opioid analgesics in properly managed patients with pain has been reported to be rare. However, data are not available to establish the true incidence of addiction in chronic pain patients." (Emphasis added.)

According to the National Institute on Drug Abuse (NIDA): "Most patients who are prescribed opioids for pain, even those undergoing long-term therapy, do not become addicted to the drugs." Further, experts who treat and study these patients concur that addiction is rare when patients are appropriately treated for pain with opioids.

We agree with FDA that there are no data to accurately characterize the extent of addiction. But it is clear that responsible medical practice rejects the idea of avoiding the use of these drugs in appropriate patients because of the fear of addiction. "Addiction is a primary, chronic, neurobiologic disease, with genetic, psychosocial, and environmental factors influencing its development and manifestations. It is characterized by behaviors that include one or more of the following: impaired control over drug use, compulsive use, continued use despite harm, and craving." (American Society of Addiction Medicine, American Academy of Pain Medicine and American Pain Society, 2001.) We believe that many of the reports (perhaps the reports to which you refer in your letter) are in actuality "physical dependence" and "withdrawal" which are normal and expected results of the abrupt cessation of therapy with opioid analgesics. In fact, physical dependence is common in dozens of drugs used for durations of weeks or more including virtually all hormones, most CNS drugs, caffeine, antiarrythmics, some antihypertensives, nasal decongestants, antianginal agents, and many more. Each of these drugs should be tapered and not abruptly discontinued. Doctors are well aware of this. In most cases, patients who no longer require a medication to which they are physically dependent can be easily weaned from the drug by gradual discontinuance under the direction of a physician. We would very much like to discuss this further with you so that we have a common understanding of our view and yours concerning the subject of addiction.

21. The letter indicates that Purdue's adoption of one or more of your proposals will negatively affect the Company's sales of OxyContin, and that this is a short-term consequence which Purdue must accept. This has already become the reality. As we told you when we last met, in the 100 counties where we believe that there is risk of OxyContin abuse and diversion, we have halted the marketing of the drug and applied our resources primarily to teaching physicians how to avoid abuse and

diversion of the product. Clearly, like the many other programs we have instituted, this will have a negative impact on our sales.

In addition, this spring Purdue voluntarily suspended shipment of the 160 mg. tablet of OxyContin—the strongest dose of OxyContin. We did this after law enforcement reported that 160 mg. tablets had been found on suspected drug dealers. Suspending shipment of that dosage strength was a substantive effort to avoid a public health problem. Such effort cannot be viewed as cosmetic.